We have for the first time, using a rapid isolation protocol of EBV-specific T cells, treated and cured a patient suffering from PTLD with multiple associated tissue lesions, using her haplo-identical mother as a donor. This treatment approach paves way for a new possibility to within days treat patients with life-threatening EBV-associated malignancies.

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ALLOGENEIC STEM CELL TRANSPLANTATION WITH REDUCED INTENSITY CONDITIONING AS TREATMENT FOR MATURE T-CELL LYMPHOMAS

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Background: For aggressive lymphomas a T-cell phenotype confers a poor prognosis. Current therapeutic strategies for T-cell non-Hodgkin lymphoma (NHL) are poorly defined. Allogeneic stem cell transplantation (Allo-HCT) is a potentially curative option but associated with high non-relapse mortality (NRM). Reduced intensity conditioning (RIC) is designed to minimize NRM while using the benefits of the graft-versus-lymphoma effect. Here we report retrospective analysis of patients with T-cell NHL who underwent Allo-HCT with RIC using fludarabine and melphalan.

Patients and Methods: A consecutive case-series of 27 patients with mature T-cell NHL were included. All patients underwent RIC with fludarabine and melphalan. Histologies included: PTCL NOS (n = 5); AILD (n = 3); ALCL (n = 2; both alk+); rare histologies (n = 6) (NK/T cell, enteropathy type, hepatosplenic); and cutaneous T-cell lymphomas (n = 11). Most patients (n = 18, 67%) had advanced disease at the time of transplant: relapse/induction failure = 17, progression = 1. The rest of the patients were in CR1 = 1, CR2 = 5, PR = 3. The median age was 50 years (range: 19-68), 74% were male (n = 20). The time from diagnosis to transplant for majority of the patients (n = 20, 74%) was more than one year. The median number of prior regimens was 4 (range: 1-9); one patient had a prior autologous transplant. All patients received stem cells, 56% from HLA-matched sibling and 44% from matched unrelated donor. 18 patients (67%) received GVHD prophylaxis with sirolimus/tacrolimus, while 9 patients (33%) received cyclosporine/cellcept based prophylaxis.

Results: The median follow-up for the 16 (59%) surviving patients was 24.2 months (range: 5.6-95.3). Day 100 mortality was 22% (n = 6). There were a total of 11 deaths; 5 from disease progression/relapse and 6 from non-relapse causes. 13 patients (48%) experienced acute GVHD: grade I = 4, grade II = 5, grade IV = 4. Among the 17 patients who are evaluable for chronic GVHD, 11 (63%) patients developed an extensive GVHD. The 2-year probability of overall (OS) and disease-free (DFS) survival were 55% (95%CI: 43-65%) and 43% (95%CI: 34-52%) respectively. The relapse/progression and NRM rates at 2 years were 37% (95%CI: 26-52%) and 28% (95%CI: 16-46%) respectively.

Conclusion: The overall results show that good long term survival rates and disease control can be achieved with acceptable non-relapse mortality in patients with mature T-cell lymphomas using reduced intensity conditioning.

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THE IMPORTANCE OF TIMING OF HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) IN PATIENTS WITH T-CELL LYMPHOMAS (T-NHL)

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Patients (pts) with T-NHL have a poor prognosis with standard chemotherapy. HSCT have been used in their management but the most appropriate time for HSCT is not clear. We previously reported the poor outcome of pts with ALK negative (anaplastic lymphoma kinase) anaplastic large cell lymphoma (ALCL) having HSCT after first recurrence (Zamkoff et al, BMT 33:635-8,2004). To further investigate outcomes of pts transplanted for T-NHL, we retrospectively analyzed 33 pts undergoing autologous HSCT from August 2000 to July 2009. 23 were male, 10 female; median age was 53.2 (29 -73) years at time of HSCT. Subtypes of T-NHL included Alk negative ALCL (9) and Alk positive ALCL (1); peripheral T-Cell (PTCL), not otherwise specified (11); Angioimmunoblastic (AILT) (9); Nasal NK/T (2) and cutaneous T-cell (CTCL) (1). 6 pts were in their first complete remission (CR1), 1 in CR1 unconfirmed (CRU1), 10 in first partial remission (PR1), 9 in first relapse (Rel1) with 8 sensitive and 1 refractory, 3 in CR2, and 4 in second or later sensitive relapse (Rel2+). Preparative regimens for HSCT included Cy/TBI (13) or Cy/etoposide/TBI (9), Bu/Cy (6), CBV (4), and BEAM (1).

Among the 12 pts in CR1/CRU1 or PR1 < 200 days from diagnosis (Group 1), there were 2 with Alk negative ALCL, 5 PTCL, 4 AILT, and 1 Nasal NK/T. Among the 21 pts (Group 2), there were 7 with Alk negative ALCL, 1 Alk positve ALCL, 6 PTCL, 5 AILT, 1 Nasal NK/T, and 1 CTCL.

With a median follow-up of 17.6 (0.4-84.0) months post HSCT, the overall survival (OS) is estimated to be 52% and progression free survival (PFS) is 45%. 16 pts have expired. Causes of death include relapse (12), transplant related mortality (1), second malignancy (1), and unknown (2) since no MD follow-up records available.

Among the 17 surviving pts, 10 were among the 12 pts in Group 1. For this group, the OS is 83% with a PFS of 75% at a median follow-up of 18.6 (0.7-60.5) months. 7 additional pts survive among the Group 2 pts; their OS is 33% and PFS is 29% at a median follow-up of 15.2 (13-84) months. In Group 2, surviving pts include 1 of 3 transplanted in CR2; 6 of 13 transplanted in Rel1 or Rel2+ and 0 of 5 in PR1 transplanted >200 days from diagnosis.

In summary, this data would suggest an improved outcome for HSCT in pts with T-NHL when applied earlier in the course of their disease. Such a strategy should be evaluated in a larger prospective trial of HSCT in CR1/PR1 to evaluate the efficacy and safety across the various subtypes T-NHL.

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PREFERENCE OF PATIENTS AND PHYSICIANS CONCERNING TREATMENT OPTIONS FOR RELAPSED FOLLICULAR LYMPHOMA: A DISCRETE CHOICE EXPERIMENT

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Background: Patients with symptomatic relapsed follicular lymphoma, together with their physicians, must choose between a variety of treatment options. The purpose of this study was to elicit relative preferences for attributes associated with different treatment options amongst lymphoma patients in Alberta, and lymphoma-treating physicians in Canada, using a discrete choice experiment (DCE).

Methods: 180 patients aged 18-65 years and 252 physicians received background information and a questionnaire containing the DCE. Treatment administration, toxicity, average remission length, and cost were the attributes evaluated for four treatment options: standard chemotherapy (CT), radioimmunotherapy (RIT), high-dose chemotherapy and autologous (AUTO) or allogeneic (ALLO) stem cell transplantation. In a series of multiple choice questions, respondents were asked to choose between two unlabeled treatment options, described according to the attributes where the attribute levels were different for each option. The DCE was analyzed using a random effects logit model. Marginal rates of substitution calculated from regression coefficients provided information about preference for the treatment attributes.

Results: 81 patients (45%) and 48 physicians (19%) completed the questionnaire. Responding patients had a mean age of 54.7 years and were on average 4.4 years from initial diagnosis. 93% of patients

received prior chemotherapy and 24% had received a prior stem cell transplant. 48% of patients had not yet relapsed and 33% were currently symptomatic. Physicians were predominantly hematologists (93%) who have been in practice on average for 12.2 years. 46% of physicians reported being in a practice that includes stem cell transplantation. For all participants, remission length was the major positive influence on choice ($p < 0.001$), and toxicity of ALLO was the major negative influence ($p < 0.001$). Cost was a significant negative influence on choice for physicians ($p = 0.001$), but not for patients. By post-estimation analysis, patients were most likely to choose AUTO (69%) and less likely to choose RIT (14%), CT (11%), and ALLO (7%). The distribution for physicians was similar.

Conclusions: Patients with relapsed follicular lymphoma are able to consider the advantages and disadvantages of various treatment options, and most are willing to trade off toxicity, hospitalization, and cost associated with autologous transplantation in order to benefit from increased remission length.

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CHRONIC GVHD AFTER ALLO-SCT WOULD BE NECESSARY FOR BETTER OUTCOME OF ALLOGENIC STEMCELL TRANSPLANTATION (ALLO-SCT) FOR CHEMOREFRACTORY NON-HODGKIN'S LYMPHOMAS -A SINGLE INSTITUTE RETROSPECTIVE STUDY

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Aims: The aims of this study are to identify the feasibility and clinical characteristics of the patients undergone Allo-SCT for chemo-refractory NHLs.

Design and methods: There were 55 NHL patients who had been undergone allo-SCT in our institute from August 2001 to March 2009 consecutively. Thirty-seven patients out of 55 were adult T-cell leukemia/lymphoma (ATLL) patients, and we analyzed about rest of 18 patents. Study endpoints were 3 years overall survival (OS), disease free survival (DFS) and these related factors.

Results: Median age was 37.5 yrs (19-63). Thirteen patients were male and 5 female. Diagnosis included FL (n = 4), PTCL-u (n = 3), MNKL (n = 3), BL (n = 2), DLBCL (n = 2), ALCL (n = 1), T-LBL (n = 1), hepatosplenic lymphoma (n = 1), and MF (n = 1). Median overall survival time and disease free survival time after SCT were 215.5 days (6-2436) and 73 days (2-2436). Overall survival rate after SCT was 38.9%. IPI was Low in 2 patients, 8 L-I, 5 H-I, and 3 High. Low/L-I group showed significantly superior OS, DFS compare to H-I/High group (54% vs 0%, 56.3% vs 0%). HCT-CI scoring 0 in 12 patients, five 1, and only one patient scored over 2. HCT-CI score significantly related to OS after SCT in our cases. There were 13 sibling donors (included 5 HLA haplo-identical donors) and 5 unrelated donors (URD) (included 2 cord blood donors) in our cases. Ten patients received myeloablative conditioning and 8 reduced intensity conditioning (RIC). Disease status at SCT was CR in 5 patients, 7 PR, and 6 PD. Eleven patients died after SCT (3 a-GVHD, 2 disease progression, 2 sepsis, 1 TMA, 1 pneumonia, 1 invasive aspergirosis, and 1 liver failure). Five patients died within 100 days after SCT. Six patients have been alive over 3 years (3 yrs OS, DFS: 33.3%, 27.8%). Seven patients were complicated grade 0-1 a-GVHD and 9 grade 2-4. Grade 0-1 group patients showed significantly superior DFS compare to grade 2-4. Five patients complained limited c-GVHD and 3 extensive. The patients group complained with c-GVHD showed better OS and DFS than asymptomatic group (53.6% vs 12.0%, 58.3% vs 12.5%). Four patients suffered relapse or progressive disease after SCT. Two out of these 4 patients showed GVL effect only with reducing immunosuppressive therapies.

Conclusion: Allo-SCT would be feasible therapy for chemorefractory NHLs. Chronic GVHD will be necessary and GVL effect would be existed in our study.

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PRESENCE OF ABNORMAL PLASMA CELLS IN PERIPHERAL STEM CELL HARVEST PRODUCTS PREDICT EARLY RELAPSE FOLLOWING AUTOLOGOUS STEM CELL TRANSPLANTATION IN PATIENTS WITH MULTIPLE MYELOMA

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Background: CD38 + 138+ stem cells more than 4.5 x10 5/kg has been found to shorten overall survival (Kopp, 2009). The EBMT report on the impact of plasma cell cytoreduction in apeheresis products has shown that despite major tumor cell elimination relapse could not be eliminated(Bourhis, 2007). Flow cytometry has been claimed to be of lesser specificity than PCR. The multiparametric flow cytometry has the potential to quantify and distinct normal plasma cells from abnormal plasma cells. The aim of this prospective study was to analyze the amount of both normal and abnormal plasma cells in peripheral stem cell products and correlate with clinical outcome.

Patients: A total of 47 consecutive multiple myeloma patients who were mobilized between March 2007 and July 2009 were included in the study. Patients were male/female: 26/21; ISS: I/II/III: 17/18/11; age: 54 (35 -65). Treatment preceding transplant consisted of novel agent including protocols (n: 13) or excluding protocols(n: 34). Plasma cell quantification was done using a panel of monoclonal antibodies by using multiparameter flowcytometry. If any aberrant expression (such as CD20(loss) CD27(loss) CD28 (gain), CD33(loss), CD34 (gain), CD81(loss), CD117(gain)) were detected at diagnosis, the corresponding antibody was also added to the panel.

Results: Abnormal plasma cells were detected in 9 apheresis products from 8 patients. The median plasma cell count (normal plus abnormal) was 6.53 (0,19-542) x 10^5/kg. In the abnormal plasma cell positive group the median total and abnormal plasma cell counts were 2.73 (0.19-542) x10^5/kg and 1.4 (0.07-542) x10^5/kg, respectively. Twenty five patients had ≥4.5 x10^5/kg (high) plasma cells while 17 patients has <4.5 x10^5/kg (low) plasma cells.Similar rate of response (> = PR) was obtained in 5/7 patients with plasma cell contamination following transplantation. Amongst 18 patients evaluable during post transplant 1 year follow up, 10 of the 12(83%) patients who had high plasma cell count and 3 of 6 (50%) patients who had low plasma cell count in their products, either progressed or relapsed.

Conclusion: High dose therapy with stem cell support may induce high hematological responses confirmed by reduction in monoclonal protein production. Patients who have lower amount of plasma cell contaminating the apheresis products seem to perform better outcome during the first year follow up after transplantation.

Table 1.

Response	Pre Mobilisation	Pre Transplant	Post Transplant month2	Relapse <1 year
Abnormal plasma cell positive	6/7	4/7	5/7	4/7
Abnormal plasma cell negative	31/34	27/34	27/32	4/13
Total	37/41	31/41	7/39	8/20

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HIGH DOSE CHEMOTHERAPY WITH AUTOLOGOUS STEM CELL TRANSPLANTATION FOR MULTIPLE MYELOMA: WHAT PREDICTS THE OUTCOME?

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We analyzed results of 118 patients (84 males and 34 females) of multiple myeloma who underwent autologous stem cell